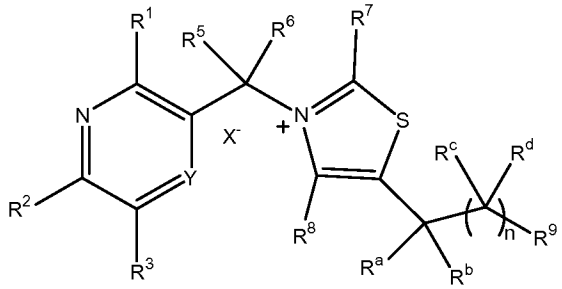
Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in the application.

1. (Original) A compound of formula I:



I

or a pharmaceutically acceptable derivative thereof, wherein:

Y is N or $C(R^4)$;

R^1 is H, alkyl, $-N(R)_2$, $-(CH_2)_{1-6}N(R°)_2$, $-(CH_2)_{1-6}OR°$, -NRC(O)R, $-C(O)N(R)_2$, -CN, $-NRSO_2R$, -COOR, -OR, -SR, -C(O)R, halo, $-OC(O)R$, -NRC(O)OR, $-OC(O)N(R)_2$, -NRC(O)NR, -NRC(S)NR, $-NRSO_2NR$, $-C(O)NRN(R)_2$, heteroaryl, or heterocyclyl;

each R^2, R^3 and R^4 is independently H, alkyl, fluoroalkyl, -C(O)R, -COOR, $-C(O)N(R)_2$, -CN, -NRC(O)R, -OR, -SR, $-N(R)_2$, $-(CH_2)_{1-6}OR°$, $-(CH_2)_{1-6}N(R°)_2$, or halo;

each R^5 and R^6 is independently H, alkyl, or fluoroalkyl;

R^7 is H, alkyl, fluoroalkyl, aralkyl, carbocyclylalkyl, heterocyclyl, carbocyclyl, heterocyclylalkyl, aryl, heteroaryl, heteroaralkyl, -C(O)R, $-(CH_2)_{1-6}OR$, $-(CH_2)_{1-6}N(R)_2$, $-C(O)CH_2C(O)R$, -NRC(O)R, $-N(R)_2$, $-C(O)N(R)_2$, or -C(H)(OR)R;

R^8 is H, alkyl, fluoroalkyl, carbocyclyl, carbocyclylalkyl, heteroaryl, heterocyclyl, $-CO_2R$, or $-CON(R)_2$;

R^9 is $-OR^{10}$ or $-NR^{11}R^{12}$;

R^{10} is R°, -C(O)R, $-C(O)N(R)_2$, -C(O)OR, $-(CH_2)_{1-6}$-C(O)R, $-PO_3M_x$, -P(O)(alkyl)OM', $-(PO_3)_2M_y$, carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl, heteroaralkyl, or a tumor-targeting moiety;

x is 1 or 2;

y is 1, 2 or 3;

each M is independently H, Li, Na, K, Mg, Ca, Mn, Co, Ni, Zn, or alkyl;

M' is H, Li, Na, K, or alkyl;

R^{11} is H or alkyl;

R^{12} is H, alkyl, -C(O)R, -C(O)N(R)$_2$, -C(O)OR, -SO_2R, -SO_2N(R)$_2$, carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl, heteroaralkyl or a tumor targeting moiety;

each R^a and R^b is independently H, OR°, alkyl, or fluoroalkyl;

each R^c and R^d is independently H, alkyl, or fluoroalkyl;

n is 0-4;

X^- is a monovalent or divalent anion, or a counterion to the thiazolium nitrogen located anywhere in the molecule;

R° is H or alkyl; and

R is R°, carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl, or heteroaralkyl;

provided that the following compounds are excluded:

Y is C(R^4);

R^5, R^6, R^a, R^b, R^c and R^d are H;

R^8 is methyl;

R^9 is -OR^{10}, and R^{10} is H, -PO_3M_x, -$(PO_3)_2M_y$ or -P(O)(alkyl)OM';

X^- is Cl^- or Br^-;

i) R^1 is H, R^2 is methyl, R^3 is -OH, R^4 is methyl, -CH_2OH or -CH_2NH_2, and R^7 is H;

ii) R^1 is -NH_2, -NHMe or -N(Me)$_2$, R^2 is methyl, R^3 is H, R^4 is H or -CH_3, and R^7 is H;

iii) R^1 is -NH_2 or OH, R^2 is methyl, R^3 is H, R^4 is H, and R^7 is H;

iv) R^1 and R^3 are H, R^2 is methyl, R^4 is -NH_2, and R^7 is H;

v) R^1 is -NH_2, R^2 is methyl, R^3 and R^4 are H, and R^7 is H, -CH(OH)CO_2H or -C(OH)(Me)CO_2H;

vi) R^1, R^3, R^4 and R^7 are H and R^2 is methyl; and

vii) R^1 is H, R^2 is $-NH_2$, R^3 is -OH, R_4 is $-CH_2CH_2NH_2$, and R^7 is H.

2. (Currently amended) The compound of **claim** 1, wherein R^{10} is -C(O)R, $-C(O)N(R)_2$, -C(O)OR, $-(CH_2)_{1-6}$-C(O)R, alkyl, carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl, heteroaralkyl, or a tumor-targeting moiety; and R^{12} is -C(O)R, $-C(O)N(R)_2$, -C(O)OR, $-SO_2R$, $-SO_2N(R)_2$, carbocyclyl, aryl, heterocyclyl, heteroaryl, carbocyclylalkyl, aralkyl, heterocyclylalkyl, heteroaralkyl or a tumor-targeting moiety.

3. (Currently amended) The compound of **claim** 1, wherein R^{10} or R^{12} is a polysaccharide, $-[C(O)CH(R)N(R)]_{2-3}$-R, an antibody, or

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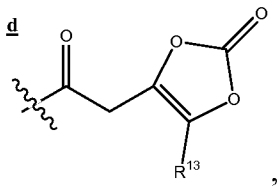

, wherein R^{13} is H, alkyl, or aryl.

4. (Canceled)

5. (Currently amended) The compound of **claim** 1, wherein:

i) R^1 is $-(CH_2)_{1-6}N(R°)_2$, $-(CH_2)_{1-6}OR°$, -NRC(O)R, $-C(O)N(R)_2$, -CN, $-N(R)SO_2R$, -COOR, -SR, -C(O)R, halo, -OC(O)R, -NRC(O)OR, $-OC(O)N(R)_2$, -N(R)C(O)N(R), -NRC(S)NR, $-NRSO_2NR$, $-C(O)NRN(R)_2$, heteroaryl, or heterocyclyl;

ii) R^2 is H, fluoroalkyl, -C(O)R, -COOR, $-C(O)N(R)_2$, -CN, -NRC(O)R, -OR, -SR, $-N(R)_2$, $-(CH_2)_{1-6}OR°$, $-(CH_2)_{1-6}N(R°)_2$, or halo;

iii) R^3 is alkyl, fluoroalkyl, -C(O)R, -COOR, $-C(O)N(R)_2$, -CN, -NRC(O)R, -SR, $-N(R)_2$, $-(CH_2)_{1-6}OR°$, $-(CH_2)_{1-6}N(R°)_2$, or halo;

iv) R^4 is fluoroalkyl, -C(O)R, -COOR, $-C(O)N(R)_2$, -CN, -NRC(O)R, -OR, -SR, $-(CH_2)_{1-6}N(R°)_2$, or halo;

v) R^{10} is H, $-PO_3M_x$, $-(PO_3)_2M_y$ or -P(O)(alkyl)OM'; or R^{12} is H or C_{1-6} alkyl; and

vi) n is 1.

6. (Canceled)

7. (Currently amended) The compound of **claim** 1, wherein:

i) R^1 is H, $-N(R)_2$, alkyl, $-NR°C(O)NR$, $-NR°C(O)OR$, $-C(O)N(R)_2$, $-(CH_2)_{1-6}N(R°)_2$, $-NR°C(O)R$, -CN, -COOR, -OR, -SR, or halo;

ii) R^2 is H, alkyl, fluoroalkyl, -OR°, $-N(R°)_2$, or halo;

iii) R^3 and R^4 are independently H, alkyl, -OR, $-N(R)_2$, $-(CH_2)_{1-6}OR°$, or $-(CH_2)_{1-6}N(R°)_2$;

iv) R^7 is H, alkyl, fluoroalkyl, $-(CH_2)_{1-6}OR$, $-(CH_2)_{1-6}N(R)_2$, $-NR°C(O)R$, -C(O)R, -C(H)(OR)R, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroaralkyl;

v) R^{10} is H, alkyl, -C(O)R, $-PO_3M_x$, -P(O)(alkyl)OM', $-(PO_3)_2M_y$, $-C(O)N(R)_2$, -C(O)OR, or a tumor-targeting moiety; or R^{12} is H, alkyl, -C(O)R, $-C(O)N(R)_2$, -C(O)OR, $-SO_2R$, 5-membered heterocyclyl, 5-membered heteroaralkyl, or a tumor-targeting moiety; and

vi) n is 1.

8. (Currently amended) The compound of **claim** 7, wherein R is R°, carbocyclyl, aryl, heteroaryl, heterocyclyl, aralkyl, keterocyclylalkyl or heteroaralkyl.

9. (Currently amended) The compound of **claim** 8, wherein R° is H or C_{1-6} alkyl optionally substituted with halo, hydroxy or amino.

10. (Currently amended) The compound of **claim** 7, wherein R^{10} or R^{12} is a polysaccharide, $-[C(O)CH(R)N(R)]_{2-3}$-R, an antibody, or

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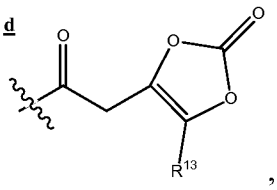


, wherein R^{13} is H, alkyl, or aryl.

11. (Currently amended) The compound of **claim** 7, wherein:

i) R^1 is H, amino, $-CH_2NH_2$, -NHC(O)NHEt, -NHC(O)OEt, $-NHCH_2OH$, $-NHCH_2CH_2OH$, $-NH-CH_2CH_2Cl$, $-N(CH_2OH)_2$, Cl, Br, $-SCH_3$, CN, $-C(O)NH_2$, -C(O)OH, methyl, or ethyl;

ii) R^2 is H, methyl, ethyl, amino, CF_3, Cl, or Br;

iii) R^3 is H, methyl, ethyl, amino, or hydroxy;

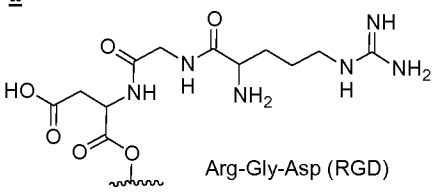
iv) R^4 is H, methyl, ethyl, $-CH_2OH$, or $-CH_2NH_2$;

v) each R^5, R^6 and R^8 is independently H, methyl, ethyl, $-CH_2F$, $-CHF_2$, or $-CF_3$;

vi) R^7 is H, methyl, ethyl, CF_3, $-CH(OH)CH_3$, $-CH_2OH$, or $-CH_2CH_2OH$; and

vii) R^{10} is H, methyl, ethyl, -C(O)Me, -C(O)Et, $-C(O)NMe_2$, -C(O)-p-OMe-phenyl, -C(O)O-phenyl, $-PO_3H_2$, $-P(O)(OMe)_2$, -P(O)(OMe)OH, -P(O)(Me)OH, -P(O)(OH)OP(O)(OH)(OH), or R^{14}; and R^{14} is selected from the group consisting of:

a

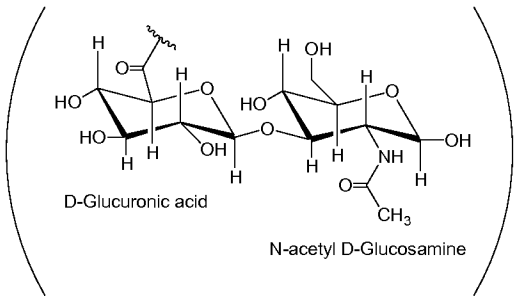


Arg-Gly-Asp (RGD)

,

b

poly



D-Glucuronic acid

N-acetyl D-Glucosamine

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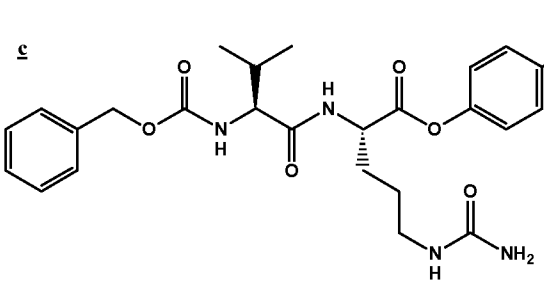
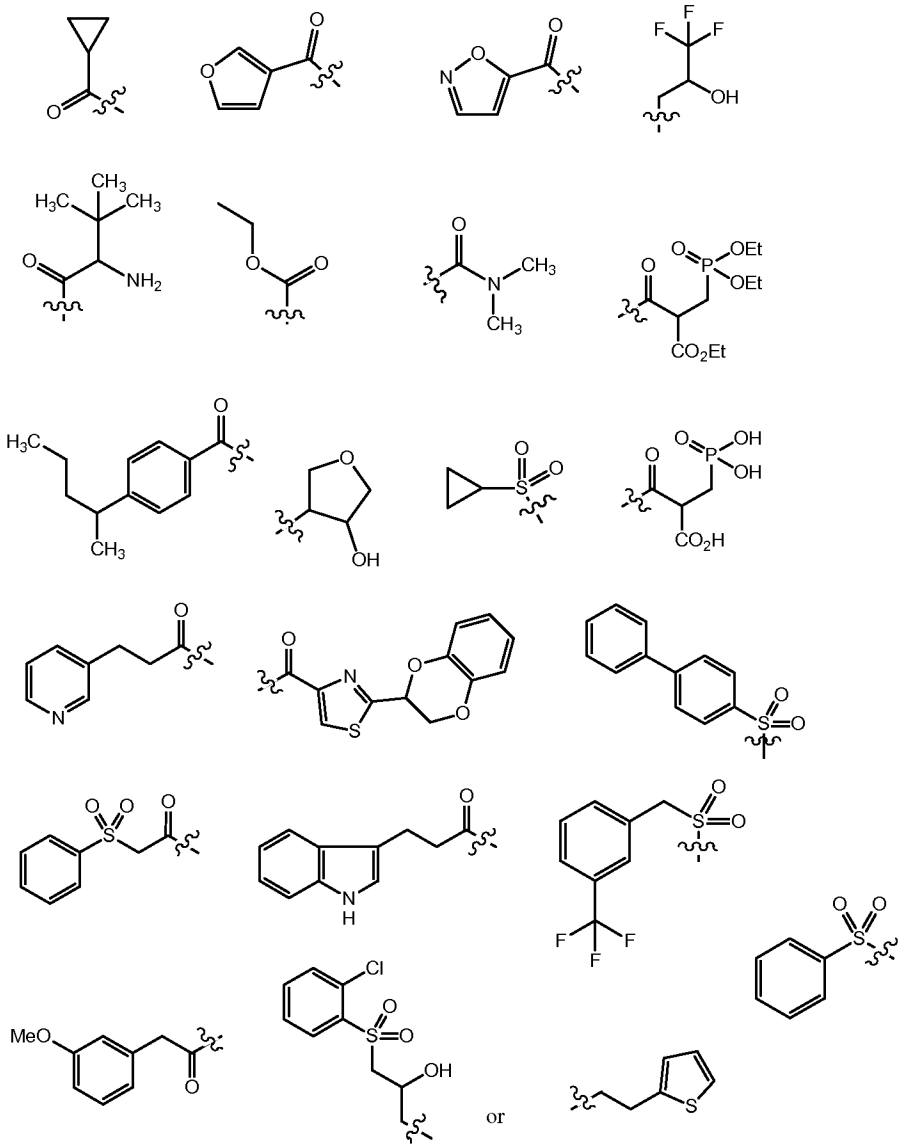
c



peptide Z-Val-Cit-PABOH

and an antibody; or R^{12} is H, methyl, ethyl, R^{14},



or

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12. (Currently amended) The compound of **claim** 7, wherein:

i) R^1 is H, $-N(R°)_2$, $-SR°$, or halo;

ii) R^2 is H, alkyl, fluoroalkyl, $-N(R°)_2$, or halo;

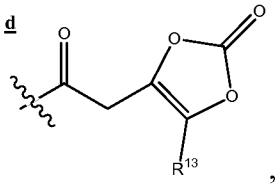
iii) R^3 and R^4 are independently H or alkyl;

iv) R^7 is H or alkyl;

v) R^8 is H or C_{1-6} unsubstituted alkyl; and

vi) R^9 is $-OR^{10}$ and R^{10} is H, C_{1-6} unsubstituted alkyl, -C(O)R, $-PO_3M_x$, -P(O)(alkyl)OM', $-(PO_3)_2M_y$, -C(O)OR, or a tumor-targeting moiety.

13. (Currently amended) The compound of **claim** 12, wherein R^{10} is a polysaccharide, $-[C(O)CH(R)N(R)]_{2-3}$-R, an antibody, or

d 

, wherein R^{13} is H, alkyl, or aryl.

14. (Currently amended) The compound of **claim** 12, wherein:

i) R^1 is H, $-NH_2$, $-SCH_3$, or Cl;

ii) R^2 is H, methyl, $-CF_3$, $-NH_2$, or Cl;

iii) R^3, R^4, R^7 and R^8 are independently H or methyl; and

iv) R^9 is $-OR^{10}$ and R^{10} is H, H, $-PO_3H_2$, $-P(O)(OMe)_2$, -P(O)(OMe)OH, -P(O)(Me)OH, -P(O)(OH)OP(O)(OH)(OH), or R^{14}; and R^{14} is as defined in 11.

15. (Currently amended) The compound of **claim** 1, wherein said compound is IIa-1, IIa-2, IIa-3, IIa-4, IIa-5, IIa-6, IIa-7, IIa-8, IIa-9, IIa-10, IIa-11, or IIc-1.

16. (Currently amended) A pharmaceutical composition comprising a compound of **claim** 1 and a pharmaceutically acceptable carrier.

17. (Currently amended) The composition of **claim** 16, further comprising at least one chemotherapeutic agent, antiangiogenic agent or agent which modulates signaling associated with hypoxic conditions in a cell.

18. (Currently amended) A method for inhibiting transketolase activity in a biological sample or a patient in need thereof comprising contacting said biological sample with or administering to said patient an effective amount of a compound of **claim** 1.

19. (Currently amended) A method for reducing levels of ribulose/ribose-5-phosphate in a cell comprising administering to the cell an effective amount of a compound of **claim** 1.

20. (Currently amended) A method for inhibiting nucleic acid synthesis in a cell comprising administering to the cell an effective amount of a compound of **claim** 1.

21. (Currently amended) A method for inhibiting cell proliferation comprising administering to the cell an effective amount of a compound of **claim** 1.

22. (Currently amended) A method for increasing apoptosis in a tumor cell comprising administering to the cell an effective amount of a compound of **claim** 1.

23. (Currently amended) A method for reducing tumor growth in a patient comprising administering an effective amount of a compound of **claim** 1 to the patient in need thereof.

24. (Currently amended) The method of **claim** 23, further comprising administering at least one chemotherapeutic agent, antiangiogenic agent or agent which modulates signaling associated with hypoxic conditions in a cell.

25. (Currently amended) The method of **claim** 23, further comprising limiting thiamine concentrations in the patient during the administration step.

26. (Currently amended) The method of **claim** 25, wherein the patient is on a reduced thiamine diet during the administration step.

27. (Currently amended) The method of **claim** 26, wherein cellular thiamine concentrations are maintained at a level sufficient to avoid toxicity associated with thiamine deficiency.